

# Exhibit 5



WORLD HEALTH ORGANIZATION

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

**IARC MONOGRAPHS  
ON THE  
EVALUATION OF THE CARCINOGENIC  
RISKS TO HUMANS**

**Overall Evaluations of Carcinogenicity: An Updating  
of *IARC Monographs* Volumes 1 to 42**

**SUPPLEMENT 7**

LYON, FRANCE

1987



WORLD HEALTH ORGANIZATION  
INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

**IARC MONOGRAPHS**  
**ON THE**  
**EVALUATION OF**  
**CARCINOGENIC RISKS**  
**TO HUMANS**

**Overall Evaluations of Carcinogenicity:**  
**An Updating of *IARC Monographs***  
**Volumes 1 to 42**

*SUPPLEMENT 7*

This publication represents the views and expert opinions  
of an IARC *ad-hoc* Working Group on the  
Evaluation of Carcinogenic Risks to Humans,  
which met in Lyon, 10-18 March 1987

1987

## IARC MONOGRAPHS

In 1969, the International Agency for Research on Cancer (IARC) initiated a programme on the evaluation of the carcinogenic risk of chemicals to humans involving the production of critically evaluated monographs on individual chemicals. In 1980 and 1986, the programme was expanded to include the evaluation of carcinogenic risks associated with exposure to complex mixtures and other agents.

The objective of the programme is to elaborate and publish in the form of monographs critical reviews of data on carcinogenicity for agents to which humans are known to be exposed, and on specific exposure situations; to evaluate these data in terms of human risk with the help of international working groups of experts in carcinogenesis and related fields; and to indicate where additional research efforts are needed.

This programme is supported by PHS Grant No. 5 UO1 CA33193-05 awarded by the US National Cancer Institute, Department of Health and Human Services. Additional support for the production of this volume was provided by the Commission of the European Communities.

©International Agency for Research on Cancer 1987

ISBN 92 832 1411 0

ISSN 0250-9555

All rights reserved. Application for rights of reproduction or translation, in part or *in toto*, should be made to the International Agency for Research on Cancer.

Distributed for the International Agency  
for Research on Cancer by the Secretariat of the  
World Health Organization

PRINTED IN THE UK

## CONTENTS

NOTE TO THE READER ..... 11

LIST OF PARTICIPANTS ..... 13

### PREAMBLE

Background .....	17
Objective and scope .....	17
Selection of topics for monographs .....	18
Data for monographs .....	18
The Working Group .....	19
Working procedures .....	19
Exposure data .....	20
Biological data relevant to the evaluation of carcinogenicity to humans .....	21
Evidence for carcinogenicity in experimental animals .....	22
Other relevant data in experimental systems and humans .....	24
Evidence for carcinogenicity in humans .....	25
Summary of data reported .....	28
Evaluation .....	29

### OVERALL EVALUATIONS OF CARCINOGENICITY

INTRODUCTION ..... 37

METHODS ..... 38

RESULTS AND CONCLUSIONS ..... 40

Table 1. Overall evaluations of carcinogenicity to humans ..... 56

### SUMMARIES AND EVALUATIONS OF EVIDENCE FOR CARCINOGENICITY IN HUMANS AND IN EXPERIMENTAL ANIMALS, AND SUMMARIES OF OTHER RELEVANT DATA, FOR AGENTS FOR WHICH THERE ARE DATA ON CARCINOGENICITY IN HUMANS

Acetaldehyde .....	77
Acrolein .....	78
Acrylonitrile .....	79
Actinomycin D .....	80

Adriamycin .....	81
Aflatoxins .....	82
Aldrin .....	88
Aluminium production .....	89
4-Aminobiphenyl .....	91
Amitrole .....	92
Anaesthetics, volatile .....	93
Androgenic (anabolic) steroids .....	96
Aniline .....	99
Arsenic and arsenic compounds .....	100
Asbestos .....	106
Attapulgite .....	117
Auramine (technical-grade) and manufacture of auramine .....	118
Azathioprine .....	119
Benzene .....	120
Benzidine .....	123
Benzidine-based dyes .....	125
Benzoyl chloride .....	126
Beryllium and beryllium compounds .....	127
Betel quid with tobacco and betel quid without tobacco .....	128
<i>N,N</i> -Bis(2-chloroethyl)-2-naphthylamine (Chlornaphazine) .....	130
Bis(chloromethyl)ether and chloromethyl methyl ether (technical-grade) .....	131
Bitumens and extracts of steam-refined and air-refined bitumens .....	133
Bleomycins .....	134
Bracken fern .....	135
1,3-Butadiene .....	136
1,4-Butanediol dimethanesulphonate (Myleran) .....	137
Cadmium and cadmium compounds .....	139
Carbon blacks and carbon-black extracts .....	142
Carbon tetrachloride .....	143
Chlorambucil .....	144
Chloramphenicol .....	145
Chlordane/Heptachlor .....	146
$\alpha$ -Chlorinated toluenes .....	148
Chlorodifluoromethane .....	149
Chloroethyl nitrosoureas: .....	150
Bischloroethyl nitrosourea (BCNU)	
1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU)	
1-(2-Chloroethyl)-3-(4-methylcyclohexyl)-1-nitrosourea (Methyl-CCNU)	

Chloroform .....	152
Chlorophenols .....	154
Chlorophenoxy herbicides .....	156
Chloroprene .....	160
Cholesterol .....	161
Chromium and chromium compounds: .....	165
Chromium metal	
Trivalent chromium compounds	
Hexavalent chromium compounds	
Chrysoidine .....	169
Cisplatin .....	170
Clofibrate .....	171
Clomiphene citrate .....	172
Coal gasification .....	173
Coal-tar pitches .....	174
Coal-tars .....	175
Coke production .....	176
Creosotes .....	177
Cyclamates .....	178
Cyclophosphamide .....	182
Dacarbazine .....	184
Dapsone .....	185
DDT .....	186
Diazepam .....	189
1,2-Dibromo-3-chloropropane .....	191
<i>ortho</i> -Dichlorobenzene and <i>para</i> -dichlorobenzene .....	192
3,3'-Dichlorobenzidine .....	193
Dichloromethane .....	194
1,3-Dichloropropene (technical-grade) .....	195
Dieldrin .....	196
Diethyl sulphate .....	198
3,3'-Dimethoxybenzidine ( <i>ortho</i> -Dianisidine) .....	198
Dimethylcarbamoyl chloride .....	199
Dimethyl sulphate .....	200
1,4-Dioxane .....	201
Epichlorohydrin .....	202
Erionite .....	203
Ethylene dibromide .....	204

Ethylene oxide .....	205
Ethylene thiourea .....	207
Fluorides (inorganic, used in drinking-water) .....	208
5-Fluorouracil .....	210
Formaldehyde .....	211
Haematite and ferric oxide: .....	216
Ferric oxide	
Haematite	
Underground haematite mining with exposure to radon	
Hexachlorobenzene .....	219
Hexachlorocyclohexanes .....	220
Hydralazine .....	222
Hydrazine .....	223
Iron and steel founding .....	224
Iron-dextran complex .....	226
Isonicotinic acid hydrazide (Isoniazid) .....	227
Isopropyl alcohol manufacture (strong-acid process), isopropyl alcohol and isopropyl oils .....	229
Lead and lead compounds: .....	230
Lead and inorganic lead compounds	
Organolead compounds	
Leather industries:	
Boot and shoe manufacture and repair .....	232
Leather goods manufacture .....	235
Leather tanning and processing .....	236
Magenta and manufacture of magenta .....	238
Melphalan .....	239
6-Mercaptopurine .....	240
Methotrexate .....	241
5-Methoxypsoralen .....	242
8-Methoxypsoralen (Methoxsalen) plus ultraviolet radiation .....	243
Methyl bromide .....	245
Methyl chloride .....	246
4,4'-Methylene bis(2-chloroaniline) (MOCA) .....	246
4,4'-Methylene bis(2-methylaniline) .....	248
<i>N</i> -Methyl- <i>N'</i> -nitro- <i>N</i> -nitrosoguanidine (MNNG) .....	248
Metronidazole .....	250
Mineral oils: .....	252
Untreated and mildly-treated oils	
Highly-refined oils	

MOPP and other combined chemotherapy including alkylating agents .....	254
Mustard gas (Sulphur mustard) .....	259
1-Naphthylamine .....	260
2-Naphthylamine .....	261
1-Naphthylthiourea (ANTU) .....	263
Nickel and nickel compounds .....	264
Nitrogen mustard .....	269
Ochratoxin A .....	271
Oestrogens, progestins and combinations .....	272
Oestrogens	
Nonsteroidal oestrogens .....	273
Diethylstilboestrol .....	273
Steroidal oestrogens .....	280
Oestrogen replacement therapy .....	280
Progestins .....	289
Medroxyprogesterone acetate .....	289
Oestrogen-progestin combinations .....	296
Sequential oral contraceptives .....	296
Combined oral contraceptives .....	297
Oestrogen-progestin replacement therapy .....	308
Phenacetin and analgesic mixtures containing phenacetin .....	310
Phenazopyridine hydrochloride .....	312
Phenelzine sulphate .....	312
Phenobarbital .....	313
Phenylbutazone .....	316
<i>N</i> -Phenyl-2-naphthylamine .....	318
Phenytoin .....	319
Polybrominated biphenyls .....	321
Polychlorinated biphenyls .....	322
Prednisone .....	326
Procarbazine hydrochloride .....	327
Propylene oxide .....	328
Propylthiouracil .....	329
Reserpine .....	330
The rubber industry .....	332
Saccharin .....	334
Shale-oils .....	339
Silica:	341
Crystalline silica	
Amorphous silica	

Soots .....	343
Spironolactone .....	344
Styrene .....	345
Sulfafurazole (Sulphisoxazole) .....	347
Sulfamethoxazole .....	348
Talc not containing asbestos and talc containing asbestos ..	349
2,3,7,8-Tetrachlorodibenzo- <i>para</i> -dioxin (TCDD) .....	350
1,1,2,2-Tetrachloroethane .....	354
Tetrachloroethylene .....	355
Tobacco products, smokeless .....	357
Tobacco smoke .....	359
<i>ortho</i> -Toluidine .....	362
Treosulphan .....	363
Trichloroethylene .....	364
4,5',8-Trimethylpsoralen .....	366
Tris(aziridinyl)- <i>para</i> -benzoquinone (Triaziquone) .....	367
Tris(1-aziridinyl)phosphine sulphide (Thiotepa) .....	368
Tris(2,3-dibromopropyl)phosphate .....	369
Uracil mustard .....	370
Vinblastine sulphate .....	371
Vincristine sulphate .....	372
Vinyl chloride .....	373
Vinyldene chloride .....	376
Wollastonite .....	377
Wood industries	
Carpentry and joinery .....	378
Furniture and cabinet making .....	380
Lumber and sawmill industries (including logging) .....	383
Pulp and paper industry .....	385

**ADDITIONAL SUMMARIES AND EVALUATIONS OF EVIDENCE FOR CARCINOGENICITY IN EXPERIMENTAL ANIMALS, AND SUMMARIES OF OTHER RELEVANT DATA, FOR SELECTED AGENTS FOR WHICH THERE ARE NO DATA ON CARCINOGENICITY IN HUMANS**

Acetamide .....	389
<i>para</i> -Aminoazobenzene .....	390
Caprolactam .....	390
Griseofulvin .....	391
Gyromitrin .....	391

Methyl parathion .....	392
Sodium <i>ortho</i> -phenylphenate .....	392
APPENDIX 1. SUMMARY OF DATA ON GENETIC AND RELATED EFFECTS .....	393
SUPPLEMENTARY CORRIGENDA TO SUPPLEMENT 4.....	401
CUMULATIVE CROSS INDEX TO <i>IARC MONOGRAPHS</i> .....	403

Shale-oils  
Soots  
Talc containing asbestosiform fibres  
Tobacco products, smokeless  
Tobacco smoke  
Treosulphan  
Vinyl chloride

*Group 2A.* The Working Group concluded that the following agents are probably carcinogenic to humans:

Acrylonitrile  
Adriamycin  
Androgenic (anabolic) steroids  
Benz[a]anthracene  
Benzidine-based dyes  
Benzo[a]pyrene  
Beryllium and beryllium compounds  
Bischloroethyl nitrosourea (BCNU)  
Cadmium and cadmium compounds  
1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU)  
Cisplatin  
Creosotes  
Dibenz[a,h]anthracene  
Diethyl sulphate  
Dimethylcarbamoyl chloride  
Dimethyl sulphate  
Epichlorohydrin  
Ethylene dibromide  
Ethylene oxide  
*N*-Ethyl-*N*-nitrosourea  
Formaldehyde  
5-Methoxypsoralen  
4,4'-Methylene bis(2-chloroaniline) (MOCA)  
*N*-Methyl-*N*'-nitro-*N*-nitrosoguanidine (MNNG)  
*N*-Methyl-*N*-nitrosourea  
Nitrogen mustard  
*N*-Nitrosodiethylamine  
*N*-Nitrosodimethylamine  
Phenacetin  
Polychlorinated biphenyls  
Procarbazine hydrochloride  
Propylene oxide  
Silica, crystalline